Original Research Article

To study the ocular surface changes in patients of diabetes mellitus

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Received: 22-09-2021 / Revised: 29-10-2021 / Accepted: 30-11-2021

Abstract

Background & Method: The present study titled "To study the ocular surface changes in patients of diabetes mellitus"was done in the Department of Ophthalmology, Shyam Shah Medical College, Rewa (M.P.). A total of 350 type 2DM patients were taken in this study in which after fund us examination 133 patients were DM without DR and 217patients were DM with D. All patients were underwent complete ocular examination including visual acuity, lid, conjunctiva, cornea and investigation such as schirmer's test, TFBUT, and central corneal thickness by AS-OCT. A detailed history was taken including the chief visual complaint, history of present illness, past history, personal history with history of diabetes mellitus and medical history. General examination and systemic examination were done and all positive findings were recorded. **Result:** A significant correlation ($p<0.0001$) was found between mean TBUT values and the duration of diabetes. The mean TBUT in patients with a duration >10 years was noted to be 7.44 ± 2.66 and in patients with a duration of < 10 years was 10.84 ± 3.17. The mean TBUT values were seen to have an inverse correlation with the severity of diabetic retinopathy. Patients with no DR had the highest mean TBUT of 12.22 seconds; those with NPDR had a value of 8.27 seconds while those with PDR had a mean value of only 6.40 seconds and the difference across the three groups was statistically significant ($p<0.0001$). Correlating the Schirmer's value with duration of diabetes, we observed that the mean value in diabetic patients with more than 10 years duration (8.16 mm) was significantly lower ($p<0.0001$) than their counterparts with disease duration less than 10 years (13.78 mm). The mean Schirmer's value also showed a significant ($p<0.0001$) inverse correlation with severity of diabetic retinopathy. The highest mean value (15.86 mm) was noted in patients with no DR followed by 9.61 mm in NPDR and the lowest value of 6.66 mm in patients with PDR. Analyzing the relationship of mean CCT with duration of diabetes, it was seen that mean CCT was significantly ($p<0.0001$) higher in patients who had a disease duration of more than 10 years (572.80µ) as compared to those with a duration of less than 10 years (557.66µ). Mean central corneal thickness was also analyzed in relation to the grade of diabetic retinopathy. It was seen that the mean CCT had a direct relation with severity of retinopathy as was evidenced by increasing values from 550.62µ in no DR group to 568.34µ in NPDR group and 582.26µ in the PDR group. This difference in the measurements was statistically significant ($p<0.0001$). **Conclusion:** Present study suggest diabetes mellitus show increase schirmer's test and TFBUT value which leads to dry eye. Dry eye can lead to vision deficit, scarring, perforation of cornea and secondary bacterial infection. Diabetes mellitus have thicker cornea which mask the accurate reading of IOP in glaucoma. Corneal thickness in diabetes mellitus is also important for planning and performing refractive surgery. So, if this syndrome diagnosed earlier and treated, it will be easy to protect from its complication.

Keywords: Ocular, metabolic, diabetes mellitus & surgery.

Study Designed: Observational cross sectional study.

Introduction

Diabetes Mellitus is one of the most common metabolic disease that has become an epidemic of 21stcentury. Diabetes mellitus (DM) along with aging are probably the major risk factors responsible for ocular disease. Prevalence of diabetes mellitus in Madhya Pradesh is 3.1%.Worldwide 382 million people diagnosed with DM[1], approximately 70% suffer from some kind of corneal complications. DM also has significant detrimental effects on the morphology, physiology and clinical appearances of the human cornea.

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Diabetic changes may manifest in the corneal epithelium, basement membrane, stroma and endothelium. Diabetic corneal alterations, such as delayed epithelial wound healing, edema, recurrent erosions, neuropathy/loss of sensitivity, and tear film changes are frequent but under diagnosed complication of type 2 diabetes mellitus. Diabetes mellitus has been identified as one of leading systemic risk factor for dry eye syndrome[2]. The incidence of dry eye syndrome in diabetes is 15 to 33%. During the course of diabetes, micro vascular damage to the lacrimal gland due to hyperglycemia, reduced lacrimal innervations as a result of autonomic neuropathy, reduced trophic support to lacrimal tissue, and reduced reflex tearing due to impairment of corneal sensitivity all contribute to the altered tear film status in diabetic patients. Tearfilm stability has been shown to be reduced in patients with diabetes. Decreased goblet cell density is believed to contribute to the decrease in tear film stability in DM[3]. In DM, the increased thickness and stiffness of the cornea occurs which is possibly influenced by hyperglycaemia induced

glycosylation of collagen. Patients with DM are prone to blepharitis as well as recurrent styes resulting from infected sebaceous glands. Diabetes is associated with asymptomatic meibomian gland dysfunction (MGD), a major cause of ocular discomfort and inflammation[4]. MGD is the most prevalent cause of evaporative dry eye. Insulin stimulated the proliferation of humanmeibomian gland epithelial cells (HMGECs), whereas high glucose was found to be toxic for HMGECs. This suggests that insulin resistance/deficiency and hyperglycemia are deleterious for HMGECs. Corneal complication diabetes mellitus:- superficial punctuate keratopathy, recurrent corneal erosion, corneal endothelial damage, delay in re epithialization of cornea, dry eye syndrome, corneal neuropathy.
So in this cross sectional study we will study the ocular surface and corneal changes associated with diabetes mellitus.

Material & Method

The present study titled "To study the ocular surface changes in patients of diabetes mellitus" was done in the Department of Ophthalmology, Shyam Shah Medical College, Rewa (M.P.) from January 2018 to September 2019.
Patients of type 2 diabetes mellitus presenting to the department of Ophthalmology directly or those referred from other departments for ophthalmic examination and who fulfilled the following criteria-

Inclusion criteria

A. All patients of diabetes mellitus type 2 with or without retinopathy
B. Duration of diabetes mellitus from the time of diagnosis of at least 1 year
C. Age above 40 years

Exclusion criteria

A. Previous history of ocular surgery
B. Presence of high myopia`
C. Active inflammation
D. Pterygium
E. Entropion
F. Trichiasis
G. Corneal pathologies
H. Glaucoma
I. Those not willing to sign consent form

After selecting the study subjects, the patients were explained about the purpose of the study and their confidentiality assured. A detailed history was taken including the chief visual complaint, history of present illness, past history, personal history with history of diabetes mellitus and medical history. General examination and systemic examination were done and all positive findings were recorded.

Results

Table 1: Distribution of patients according to age

Age Group	No DR (n=133)	NPDR (n=165)	PDR (n=52)	Total (n=350)
41 – 50 years	25(18.79 %)	13 (8.7%)	0 (0%)	38 (10.85%)
51 – 60 years	61(45.86%)	98 (55.75%)	18 (34.61%)	177 (50.57%)
61 -70 years	35(26.31%)	51 (30.90%)	21(40.38%)	107 (30.57%)
>70 years	12(9.02%)	03 (1.81%)	13 (25.0%)	28 (8.0%)
Total	**133**	**165**	**52**	**350**

The age of the patients in the present study ranged between 42 years to 82 years with a mean age of 59.43+25 years. The maximum number (n=177; 50.57%) of patients overall belonged to the age group of 51-60 years. Likewise, patients with no DR (n=61: 45.86%) and those with NPDR (n=98; 55.75%) were highest in the 51-60 years age group. However, patients with PDR were maximally found in the age group of 61-70 years.The least number of patients overall (n=28; 8.0%), in the no DR (n=12; 9.02%) and NPDR groups (n=3; 1.81%) were in the > 70 years age group while in the PDR group (n=0; %) were in the 41-50 years.

Table 2: Mean TBUT according to duration of disease

Duration of Disease	No. of cases	Mean TBUT	SD	P value
>10 Years	139	7.44	±2.66	<0.0001
<10 Years	211	10.84	±3.17	

A significant correlation (p<0.0001) was found between mean TBUT values and the duration of diabetes. The mean TBUT in patients with a duration >10 years was noted to be 7.44 ± 2.66 and in patients with a duration of < 10 years was 10.84 ± 3.17.

Table 3: Mean TBUT in relation to grade of diabetic retinopathy

Group	No. of cases	Mean TBUT	SD	P value
NO DR	133	12.22	±2.57	<0.0001
NPDR	165	8.27	±2.82	
PDR	52	6.40	±1.68	

The mean TBUT values were seen to have an inverse correlation with the severity of diabetic retinopathy.Patients with no DR had the highest mean TBUT of 12.22 seconds; those with NPDR had a value of 8.27 seconds while those with PDR had a mean value of only 6.40 seconds and the difference across the three groups was statistically significant (p<0.0001).

Table 4: Mean Schirmervalue among different age groups

Age Group	No. of cases	Mean	SD	P value
41 - 50 years	38	13.85	±4.735	0.0107
51 - 60 years	177	11.66	±4.748	
61 - 70 years	107	10.90	±4.735	
> 70 years	28	10.17	±4.789	

The tear film was also assessed by Schirmer test and the mean values for each age group were noted. Like TBUT, mean Schirmer value also showed an inverse association with age. It was found to be 13.85 mm in patients of age group 41-50 years and then decreased successively from 11.66 mm in the 51-60 years age group to 10.90 mm in 61-70 years age group to come to a minimum of 10.17 mm in patients aged 70 years or more. The difference in the mean values between the different age groups was found to be statistically significant (p=0.0107).

Table 5: Mean Schirmervalueamong Male and Female patients

Gender	No. of cases	Mean	SD	P value
Male	179	11.24	±4.69	0.212
Female	171	11.87	±4.75	

On the basis of gender, the Schirmer test showed that diabetic males had a slightly lower mean value of 11.24 mm as compared to females who had a mean value of 11.87 mm, but the difference in these values was statistically insignificant (p=0.212).

Table 6: Mean Schirmer value according to duration of disease

Duration DM	No. of cases	Mean	SD	P value
>10 years	139	8.16	±3.34	<0.0001
<10 years	211	13.78	±4.16	

Correlating the Schirmer value with duration of diabetes, we observed that the mean value in diabetic patients with more than 10 years duration (8.16 mm) was significantly lower (p<0.0001) than their counterparts with disease duration less than 10 years (13.78 mm).

Table 7: Mean Schirmervalue in relation to grade of diabetic retinopathy

Group	No. of cases	Mean	SD	P value
NO DR	133	15.86	2.99	<0.0001
NPDR	165	9.61	3.64	
PDR	52	6.66	1.56	

The mean Schirmer value also showed a significant (p<0.0001) inverse correlation with severity of diabetic retinopathy. The highest mean value (15.86 mm) was noted in patients with no DR followed by 9.61 mm in NPDR and the lowest value of 6.66 mm in patients with PDR.

Table 8: Mean Central Corneal thickness among different age groups

Age Group	No. of Cases	Mean CCT	SD
41-50 years	38	554.32	±14.85
51-60 years	177	563.81	±14.9
61-70 years	107	565.43	±14.91
>70 years	28	568.80	±14.66

The mean central corneal thickness (CCT) was measured and analyzed according to the age of patients. The lowest mean CCT (554.32 ±14.85µ) was seen in patients between 41-50 years and the highest (568.30±14.66) in patients aged 70 years and more, thus inferring that the mean CCT increased with increasing age but the difference did not reach statistical significance (p=0.546)

Table 9: Mean central corneal thickness among Male and Female patients

Gender	No. of Cases	Mean CCT	SD	P value
Male	179	564.27	±14.72	0.4409
Female	171	563.04	±15.10	

Comparing the mean CCT values among male and female subjects, we found no significant difference (p=0.4409) with males having a mean thickness of 564.27 µ and females having 563.04µ.

Table 10: Mean CCT according to duration of disease

Duration of Diabetes	No. of Cases	Mean CCT	SD	P value
> 10 Years	139	572.80	±11.5543	<0.0001
< 10 Years	211	557.66	±13.7957	

Analyzing the relationship of mean CCT with duration of diabetes, it was seen that mean CCT was significantly (p<0.0001) higher in patients who had a disease duration of more than 10 years (572.80µ) as compared to those with a duration of less than 10 years (557.66µ)

Table 11: Mean Central Corneal thickness in relation to grade of diabetic retinopathy

Group	No. of cases	Mean CCT	SD	P Value
No DR	133	550.62	11.1640	<0.0001
NPDR	165	568.34	8.9843	
PDR	52	582.26	8.4855	

Mean central corneal thickness was also analyzed in relation to the grade of diabetic retinopathy. It was seen that the mean CCT had a direct relation with severity of retinopathy as was evidenced by increasing values from 550.62µ in no DR group to 568.34µ in NPDR group and 582.26µ in the PDR group. This difference in the measurements was statistically significant (p<0.0001).

Discussion

In this present study,changes oftear function parameters in Diabetes Mellitus Type 2 were studied.We did TFBUT to check the stability of Tear film and Schirmer test to check the basal tear production.

We found bothSchirmertest and TFBUT to be significantly reduced in diabetic patients. Mean Schirmer'stest value in No DR, NPDR and PDR were 15.86±2.99, 9.61±3.64 and 6.66±1.56 respectively. The difference in these values among the different groups was found to be statistically significant (p<0.0001).

Similarly, Mean the TFBUT values in No DR, NPDR and PDR groups were measured to be 12.21±2.57, 8.27±2.82 and 6.40±1.68 respectively and the difference in these values across the three groups was significant (p<0.0001). Thus it was deduced that TFBUT and Schirmer values are significantly correlated with severity of diabetic retinopathy[5].

Our findings are in accordance with Ozdemir et al(2003)[6]whoalso found mean Schirmer test values in NO DR, NPDR and PDR to be 10.25±1.52, 10.14±1.55 and 7.12±0.78 respectively and mean TFBUT values of 10.21±1.11, 9.84±0.92 and 7.47±0.53 respectively. The differences in mean values of both Schirmer (P <0.05) and TBUT (P <0.05) were statistically significant thus corroborating that both are associated with severity of DR. Murat Dogru et al (2011)[7]found mean Schirmer test value in No DR, NPDR and PDR as 9.96±4.27, 8.50±2.89 and 6.21±2.09 respectively and mean TFBUT value in No

DR, NPDR and PDR as10.03±1.27, 8.58±2.46 and 8.48±2.04 respectively. They found a significant difference in both mean schirmer's test value (P<0.001) and mean TFBUT value (P<0.001) when compared between no DR and DR but they were not related to stage of retinopathy.

In contrast,KC Yoon et al (2005)[3] who evaluated Schirmertest value and TFBUT in different diabetic groups of patients in Korea found mean Schirmertest value of 15.57±4.99, 13.04±3.93 and 9.81±2.70 in No DR, NPDR and PDR groups respectively and they also reported this difference to be statistically significant. However, themean TFBUT value in their study showed no statistically significant difference between the three groups of No DR (8.79±2.45),NPDR (8.25±1.82) and PDR (6.75±1.65). Comparable Schirmervalues and TFBUT values between diabetic patients (10.61±6.86mm) and age and gender matches controls and (10.92±7.05mm) and even worsening retinopathy had no significant (p>0.05) difference in both values. Both totaland reflex secretion as well as TFBUT values were not significantly (p>0.05) correlated with the stage of DR.

The possible mechanism for decreased tear secretion in patients with DM is damage to the microvasculature of the lacrimal gland and autonomic neuropathy, which leads to impaired lacrimal gland function.

When we analysed the effect of duration of diabetes on the tear parameters, we found TFBUT value to be significantly(p<0.0001) reduced in patients having DM >10 years (7.44±2.66) as compared to those with duration <10 years (10.84±3.17).Likewise, meanSchirmertest value in DM <10 years (13.78±4.16) and in DM > 10 years (8.16±3.34) were also significantly (p<0.0001) different. Our findings are in accordance with studies of Masoud Reza Manaviat et al (2008)[9], reported a significant correlation of tear film parameters with duration of diabetes. But in contrast to our study KC Yoon et al (2005)[3] who evaluated Schirmertest value (mm) and TFBUT value (sec) in DM>10 years and DM<10 years,found values of 12.27±5.08 and 14.06±4.89 respectively for Schirmer test and 7.58±1.85 and 8.28±2.54 respectively for TBUT and found no significant association of both with duration of disease. Similarly, Dogru et al (2011)[7] who evaluated Schirmertest value (mm) and TFBUT value (sec) in DM>10 years and DM<10 years found no significant correlation between duration and tear film parameters.

The central corneal thickness was measured by the AS-OCT and the mean values were assessed for their association with DR, age and gender and duration of diabetes.

Diabetic retinopathy

In our study, mean central corneal thickness was significantly reduced in diabetes mellitus type 2. The mean CCT in No DR, NPDR and PDR groups was measured to be 550.62±11.16, 568.34±8.98 and 582.26±8.48respectively. There was a significant difference (p<0.0001)in these mean CCT values between the three groups. Our results are comparable with Abd- Rashid Suraida et al (2018)[10] who measured CCT in type 2 DM patients using Anterior Segment Optical Coherence Tomography (AS-OCT). They found significant difference of mean CCT values between non DM and DM with NPDR (mean difference 36.14 μm, p < 0.001) and also between non DM and DM with no DR (mean difference 31.48 μm, p = 0.003).Mean CCT in No DR and DR and found the measurements to be 553.54±28.07 and 588.20±16.73 respectively, the difference for both being statistically (p<0.0001) significant thus establishing an association between CCT and severity of retinopathy.

In contrast to our studyShifa et al (2017)[11] found mean CCT values of 512.60±37.01, 509.91±28.24 and 514.55±33.30 in No DR, NPDR and PDR respectively and the difference between these was statistically insignificant (p=0.810). OkanToygar et al (2015)[12] also found no statistically significant difference between the mean CCT values in patients of No DR (552.5±38.0), NPDR (560.0±32.3) and PDR (550.1±38.3).

In our study, we found that as the age of patients increased, the mean CCT increased with highest being in age group more than 70 years (568.80±14.66) and lowest in 41-50 years age group (554.32±14.85). Although, mean CCT increased with increasing age but association of CCT with age group was found to be insignificant. We also found that mean CCT value was slightly lower in females (563.04±15.10) as compared to males (564.27±14.72) but association of CCT value with gender was found to be insignificant (P= 0.4414).Our study is comparable with OkanToygar et al (2015)[12] who evaluated mean CCT in different age (P value=0.63) and sex (P value=0.34) and found no significant difference.

Conclusion

A total of 350 type 2 DM patients were taken in this study in which after fundus examination 133 patients were DM without DR and 217 patients were DM with DR. A thorough history was taken and a comprehensive ophthalmic examination was done. All patients undergo complete ocular examination including visual acuity, lid, conjunctiva, and cornea. All patients undergo investigation such as schirmer's test, TFBUT, and central corneal thickness by AS-OCT. After the completion of study, observation thus made were discussed and following conclusion were drawn.

In our study we found Mean schirmer test value in No DR , NPDR and PDR are 15.86±4.74 , 9.61±4.73 and 6.66±4.77 respectively and significantly reduced in Diabetes mellitus type 2(Pvalue<0.0001).

In our study, Mean TFBUT value in NO DR, NPDR and PDR are 12.21±3.41, 8.27±3.41 and 6.40±3.41 respectively and significantly reduced in Diabetes mellitus type 2(Pvalue<0.0001).

In present study Mean CCT in NO DR, NPDR and PDR are 550.62±14.90, 568.34±14.90 and 582.26±14.92 respectectively and significant difference in Mean CCT in NO DR, NPDR and PDR having P value <0.0001.

In our study Mean CCT in DM >10 years and DM <10 years are 572.80±14.91 and 557.66±14.89 respectively and significant difference in Mean CCT between Diabetes and duration of disease (P value <0.0001).

In our study, As the age of patients increases, Mean CCT increases with highest being in age group more than 70 years (568.80±14.66) and lowest in 41-50 years age group (554.32±14.85) but association of CCT with age group was found to be insignificant.

In our study, we found that Mean CCT value was slightly lower in female (563.04±14.93) as compared to male (564.27±14.91) but association of CCT value with gender was found to be insignificant(P value= 0.4414).

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Conflict of Interest: Nil Source of support: Nil